

## Insulin therapy for dogs and cats

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**W**ith the recent changes in the human market, choosing an appropriate insulin preparation for diabetic dogs and cats can be confusing for the practitioner. This article summarizes the currently available insulins, their primary indications, and handling considerations. Practitioners are encouraged to review the references or current textbooks for more detailed information on the diagnosis and management of diabetic dogs and cats.

The currently available insulins (Table 1) include the human recombinant insulins (Novolin, Novo Nordisk Ltd., Mississauga, Ontario, and Humulin, Eli Lilly Canada Inc., Scarborough, Ontario), bovine/porcine insulins (Iletin, Eli Lilly Canada Inc.), and purified porcine insulins (Iletin II Pork, Eli Lilly Canada Inc.; Caninsulin, Intervet Canada, Whitby, Ontario). Only Caninsulin is labelled for veterinary use. Canine insulin is identical to porcine insulin, differs by 1 amino acid from human insulin, and differs by several amino acids from bovine insulin. Feline insulin differs by 1 amino acid from bovine insulin, but differs by several amino acids from porcine and human insulins. The types of insulin will vary in onset, peak, and duration of hypoglycemic activity. Insulin response profiles for humans are not accurate for dogs and cats. Insulin response will vary from patient to patient, but in general, duration of action is shorter in dogs and cats than in humans.

### Choosing an insulin formulation

Regular insulin (Novolin **ge** Toronto, Humulin R, Iletin Regular, Iletin II Regular) is a clear solution of zinc-insulin crystals that can be administered IV, IM, or SC. It has a rapid onset and short duration of action and is commonly used in the emergency management of diabetic ketoacidosis.

Neutral protamine hagedorn (NPH) insulins (Novolin **ge** NPH, Humulin N, Iletin NPH, Iletin II NPH) and lente insulins (Novolin **ge** Lente, Humulin L, Iletin Lente, Iletin II Lente, Caninsulin) are intermediate duration formulations. Protamine in NPH insulin enhances binding of insulin to proteins, thereby slowing absorption and metabolism. Lente insulin is a combination of semilente and ultralente insulins in a 30:70 mixture (30% amorphous insulin and 70% crystalline zinc insulin).

Ultralente insulins are formulations having a long duration of action; they are now only commercially produced as human recombinant insulins (Novolin **ge** Ultralente, Humulin U). They are a crystalline zinc

formulation of insulin, have a prolonged duration of action, and are often suitable for once daily insulin therapy.

### Dogs

In diabetic dogs, NPH insulin is commonly used to establish glycemic control. The bovine/porcine insulin is the most antigenic and, therefore, has a longer duration of action than the less antigenic purified porcine or human recombinant insulins. It may be possible to maintain some dogs with once daily therapy using Iletin NPH insulin. The other NPH and lente insulins have a rapid onset of action and a duration of effect ranging from 6 to 14 h. The human recombinant NPH or lente insulins almost always require twice daily insulin therapy.

### Cats

In diabetic cats, ultralente insulin is the maintenance treatment of choice. Ultralente insulin has a peak effect in 3 to 8 h, and a duration of activity of 8 to 20 h. In approximately 20% of cats, ultralente insulin will be ineffective due to impaired absorption, resulting in a delayed or minimal decrease in glucose concentration. Lente insulin, administered twice daily, may be effective in some cats that are not controlled well with ultralente insulin. Lente insulin is more potent than ultralente insulin; therefore, the dose of lente insulin is usually less than that of ultralente for a similar hypoglycemic effect. Lente insulin may also be ineffective in some cats because of a short duration of effect. If both ultralente and lente insulins are ineffective in establishing glycemic control in a cat, a thorough diagnostic evaluation is warranted. Causes of insulin ineffectiveness to be considered include insulin antibody formation, acromegaly, pituitary tumors, persistent stress-induced hyperglycaemia, pancreatitis, hyperthyroidism, infection, and diabetogenic medications (corticosteroids, megestrol acetate).

### Administration

#### Concentration

Insulin concentration is expressed in United States Pharmacopeia (USP) units (U). Human labelled formulations are available in 100 U/mL concentrations, while Caninsulin is available in a 40 U/mL concentration. Syringes calibrated to deliver the 40 U/mL insulin are available from Intervet Canada, but they are considerably more expensive than the standard 100 U/mL insulin syringes. It is very difficult to accurately measure out the 1 to 2 U doses needed by many small dogs and cats using 100 U/mL insulin; therefore, the insulin may

**Table 1. Insulins currently available in Canada**

	Source	Comments
Regular insulin		
Novolin <b>ge</b> Toronto	HR	All formulations have rapid onset, short duration. Used to treat ketoacidosis.
Humulin R	HR	
Iletin Regular	Cattle/pig	
Iletin II Regular	Pig	
NPH insulin		
Novolin <b>ge</b> NPH	HR	Iletin NPH first choice in dogs. HR and porcine NPH insulins have a short duration of action in cats and dogs; usually require twice daily therapy
Humulin N	HR	
Iletin NPH	Cattle/pig	
Iletin II NPH	Pig	
Lente insulin		
Novolin <b>ge</b> Lente	HR	Usual duration is 6–14 hours in dogs, 6–8 hours in cats. Usually requires twice daily therapy. Use in cats when ultralente insulin is ineffective.
Humulin L	HR	
Iletin Lente	Cattle/pig	
Iletin II Pork Lente	Pig	
Caninsulin	Pig	
Ultralente insulin		
Novolin <b>ge</b> Ultralente	HR	Insulin of first choice in cats for once daily treatment, but ineffective in 20% of cats.
Humulin U	HR	

HR — Human recombinant

NPH — Neutral protamine hagedorn

need to be diluted. Insulin can be diluted with 0.9% sodium chloride or USP Water for Injection, but the diluted insulin is only stable for 24 h. For maintenance therapy, insulin diluents can be formulated by a pharmacy familiar with the procedure or appropriate diluents for the human recombinant and Iletin insulins can be obtained from the manufacturers (Appendix 1). Diluents are formulated for the type of insulin (Regular, NPH, Lente series), regardless of the origin of the insulin (human vs. animal). Diluted insulins should be kept refrigerated and discarded after 30 d.

### Handling

Because it is a protein, insulin is damaged by temperature extremes. Unopened vials should be refrigerated and kept from freezing. Insulin should be mixed gently by rolling the bottle between the palms; vigorous shaking can denature the insulin and causes the product to foam, making accurate measurement difficult. Clients should be warned not to reuse insulin syringes, as the silicon coating inside the syringe can contaminate the insulin vial with silicon. This forms a white precipitate and may interfere with the biologic activity of the injected insulin. Improper handling that results in loss of potency will lead to therapeutic failure. The practitioner should suspect this if continual dose adjustments seem necessary. Dispensing or prescribing a fresh vial of insulin and careful review of handling and administration procedures with the client can correct this problem.

Pen delivery devices for insulin may be useful for some veterinary patients and their owners (Appendix 2). The Novolin-Pen (Novo Nordisk Inc.) comes in 2 sizes: 1.5 mL for use with Novolin **ge** Toronto and 3.0 mL for Novolin **ge** Toronto or NPH insulin. It allows clients to “dial a dose” and accurately administer it without having to separately handle insulin vials, syringes, and needles. The BD-Pen (Eli Lilly Canada Inc.) is for use

with 1.5 mL Humulin R and Humulin N cartridges. Insulin cartridges for lente or ultralente insulins are not available for use with the pens.

### Changing insulins

It must be strongly emphasized that each patient's response to a brand or type of insulin is unique, so the practitioner should reestablish the patient's glucose response curve anytime insulin therapy is altered. As human insulin only differs by 1 amino acid from canine insulin, switching a dog from bovine/porcine insulin to human recombinant insulin may require a decrease in dose and almost always requires increased frequency of administration. In the cat, purified porcine and recombinant human insulins are presumably antigenic, but the frequency of insulin antibody-induced insulin resistance appears low in the cat.

### Summary

Management of diabetic dogs and cats requires a tremendous cooperative effort between the practitioner and the client. Consistency in the handling, availability, and formulations of the different insulins will improve client compliance. In addition to insulin therapy, successful management of the diabetic animal includes the client's perceptions of the animal's health, maintenance of the animal's body weight, consistency in water consumption, and monitoring serial blood glucose concentrations. Serial blood glucose determinations improve the practitioner's ability to identify and address problems associated with insulin therapy, and thereby delay or minimize the complications of long-term diabetes.

### Appendix 1.

Diluents for Novolin insulins may be ordered from Novo Nordisk Inc. by calling 1-800-465-4334. Diluents

for Lilly insulins may be ordered from Eli Lilly Canada Inc. by calling 416-694-3221 or 1-800-268-4446.

Diluent made to order for NPH, lente and ultralente insulins can be ordered from The Veterinary Pharmacy, 178 Alma Street, Guelph, Ontario, N1K 1A8, 519-856-2065. Please allow 3 weeks for preparation.

## Appendix 2.

Information for obtaining pen delivery devices.

Novolin-Pen: contact Novo Nordisk Inc. Consumer Information at 1-800-465-4334.

BD-Pen: contact Eli Lilly Medical Information at 1-800-268-4446.

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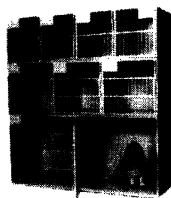
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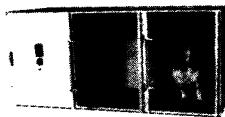
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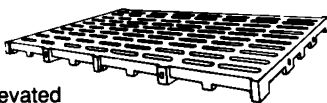
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